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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,905	02/18/2004	Daniel Paris	12062.105006 (RSK006)	7571

20786 7590 09/25/2006

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EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 09/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/780,905	PARIS ET AL.	
	Examiner	Art Unit	
	Marcela M. Cordero Garcia	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,15,20-24,26-28,30-38, 45 and 60-70* is/are pending in the application.

4a) Of the above claim(s) *32-38* is/are withdrawn from consideration.

5)☒ Claim(s) *1* is/are allowed.

6)☐ Claim(s) *15,20-24,26-28,45 and 60-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

This Office Action is in response to the reply received on June 13, 2006.

Claims 1,15, 20-24, 26-28, 30-38, 45 and 60-70 are pending in the application. Claims 31-38 are withdrawn as not drawn to either Applicant's (L-685,458) nor Examiner's (DAPT) elected species.

Any rejection from the previous office action, which is not restated here, is withdrawn.

Specification

The disclosure stands objected to because of the following: This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 1(a)(1) and (a)(2) (see, e.g., paragraph 52). However, this application fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825 for the reason(s) set forth on the attached Notice to Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Appropriate correction is required.

A revised sequence listing in computer readable form (CRF) was provided by Applicant on June 13, 2006. However, the CRF provided was not compliant, as indicated in a Raw Sequence Listing Error Report letter attached to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15, 20-24, 26-28, 30-31, 45 and 60 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific secretase inhibitors such as L-685,458, DAPT and DAPM, JLK-6, OM99-2, Z-VLL-CHO, GL189 and P10-P4'statV, does not reasonably provide enablement for any and all secretase inhibitors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims, which includes any and all protease inhibitors.

With regards to protease inhibitors and their properties, the art is unpredictable. Shearman et al. (Biochem, 2000) state, "Specific and potent inhibitors of AßPP (amyloid beta-protein precursor) gamma secretase activity such as L-685,458 will enable important advances toward the identification and elucidation of the mechanism of action of this *enigmatic* protease".

Further, as Applicant readily admits in page 13 of their reply dated September 30, 2005, "the mechanism by which gamma secretase inhibitors inhibit angiogenesis may not be via inhibition of Notch signaling in endothelial cells at all, but due to some other, as yet unidentified mechanism".

Given that one could not determine a general mechanism of anti-angiogenic action for all protease inhibitors, that gamma proteases themselves are highly enigmatic, and given the breadth of the working examples provided, it flows logically that one would be unduly burdened with experimentation to determine the effect of any

and all protease inhibitors (including any proteases created by substitution of groups therein) in regards to their anti-angiogenic properties and in order to use/make the instantly claimed therapeutic invention.

All other claims that depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, second paragraph for the reasons set forth above.

Applicant argues that the claimed methods are not directed to the use of a broad class of protease inhibitors, but rather to methods of administration of secretase inhibitors and that one skilled in the art would not be unduly burdened with experimentation to practice the claimed invention.

Applicant's arguments have been fully considered but they are not persuasive for the reasons of record above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15, 20-27, 30-31, 45 and 60-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jundt et al. (Blood, November 16, 2002)

Jundt et al. teach a method of treating a tumor (Hodgkin and Anaplastic Large Cell Lymphoma) comprising administering to the animal or human a therapeutically effective amount of a composition comprising a carrier and at least one secretase inhibitor (DAPT). Jundt et al. also teach that gamma-secretases in general, including DAPT might be a novel therapeutic principle to control the proliferation capacity of neoplasms (See entire abstract, Blood 2002, Vol. 100, No. 11, page 158a). Please note that the instantly claimed anti-angiogenic effect would be inherent to such method.

Jundt et al. do not expressly teach an in vivo method or treating a solid tumor with the secretase inhibitor.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Jundt et al. by applying it to solid tumors, which are a type of neoplasm. The skilled artisan would have been motivated to do so because Jundt et al. teaches that gamma secretases might control neoplasms (i.e., reduce volume). There would have been a reasonable expectation of success, given

that DAPT had shown tumor cell growth in vitro as taught by Jundt et al. (last paragraph). The adjustment of particular conventional working conditions (e.g., determining type of neoplasm to be treated within this therapeutic method) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. Thus, the invention as a whole is prima facie obvious over the references, especially in the absence of evidence to the contrary.

Applicant's arguments that the reference cited only teaches hematopoietic malignancies, not solid tumors, wherein inhibition of angiogenesis would not apply have been carefully considered, yet not deemed persuasive for the reasons set forth above.

Claims 15, 20-27, 30-31, 45, 60-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weng et al. (Mol. Cell. Biol., January 2003).

Weng et al. beneficially teach a method of treating a tumor by inhibiting angiogenesis comprising administering to the animal or human a therapeutically effective amount of a secretase inhibitor effective to inhibit angiogenesis and to reduce tumor volume. (See, e.g., abstract, page 656, column 2, lines 28-38, 57-75, page 657, column 1, lines 2-6, 23-35, page 662, column 2, lines 13-16, page 663, column 1, lines 1-59, column 2, lines 1-17, Figs. 2-8).

Weng et al. do not expressly teach an in vivo method of treating a tumor in an animal or human in need thereof and using a carrier in addition to the secretase inhibitor and/or expressly selecting DAPT from amongst the secretase inhibitors listed therein.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to adjust particular conventional working conditions within such method of treating cancer (e.g., expressly selecting DAPT as the secretase inhibitor, carrying out in vivo administration of such inhibitors using various modes of administration known in the art and/or treating different types of solid tumor growths) based upon the overall beneficial teachings provided by Weng et al. since Weng teaches that DAPT and analogous secretase inhibitors specifically induce growth suppression and apoptosis of murine pre-T acute lymphoblastic leukemia cells in vitro and that this step is a potential target for chemotherapeutic intervention. (See citations above). These types of adjustments are deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. Thus, the invention as a whole is prima facie obvious over the reference, especially in the absence of evidence to the contrary.

Applicant's arguments that the reference cited only teaches hematopoietic malignancies, not solid tumors, wherein inhibition of angiogenesis would not apply have been carefully considered, yet not deemed persuasive for the reasons set forth above.

Conclusion

Claims 1 is allowed.

Claims 15, 20-24, 26-28, 30-31, 45 and 60-70 are rejected.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcela M. Cordero Garcia whose telephone number is (571) 272-2939. The examiner can normally be reached on M-Th 7:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marcela M Cordero Garcia, Ph.D.
Patent Examiner
Art Unit 1654

MMCG 09/06

Cecilia J. Tsang
Supervisory Patent Examiner
Technology Center 1600

Notice to Comply	Application No. 10/780,905	Applicant(s) Paris et al.	
	Examiner M.M.Cordero Garcia	Art Unit 1654	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☒ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: The disclosure and claims are missing numbers SEQ ID NO:s, see attached Action under Sequence Compliance.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

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